



Complete Summary

GUIDELINE TITLE

Long-term management of asthma.

BIBLIOGRAPHIC SOURCE(S)

Finnish Medical Society Duodecim. Long-term management of asthma. In: EBM Guidelines. Evidence-Based Medicine [CD-ROM]. Helsinki, Finland: Duodecim Medical Publications Ltd.; 2004 Apr 8 [Various]. [103 references]

COMPLETE SUMMARY CONTENT

SCOPE
METHODOLOGY - including Rating Scheme and Cost Analysis
RECOMMENDATIONS
EVIDENCE SUPPORTING THE RECOMMENDATIONS
BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS
IMPLEMENTATION OF THE GUIDELINE
INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT
CATEGORIES
IDENTIFYING INFORMATION AND AVAILABILITY

SCOPE

DISEASE/CONDITION(S)

Asthma

GUIDELINE CATEGORY

Evaluation
Management
Treatment

CLINICAL SPECIALTY

Family Practice
Internal Medicine
Pulmonary Medicine

INTENDED USERS

Health Care Providers
Physicians

GUIDELINE OBJECTIVE(S)

Evidence-Based Medicine Guidelines collect, summarize, and update the core clinical knowledge essential in general practice. The guidelines also describe the scientific evidence underlying the given treatment recommendations.

TARGET POPULATION

Patients with asthma

INTERVENTIONS AND PRACTICES CONSIDERED

Non-Pharmacologic Interventions

1. Patient education in self-management (inhalation techniques, drug dosing, use of peak expiratory flow meter) and regular practitioner review
2. Sanitary measures, such as avoidance of allergens, sensitizing chemicals
3. Smoking cessation
4. Caution in use of aspirin and other nonsteroidal anti-inflammatory drugs and beta-blockers
5. Desensitisation therapy
6. Physical training and breathing exercises
7. Specialist consultation, as indicated

Note:

- Guideline developers considered influenza vaccination; however, they did not find enough evidence to evaluate the benefits of influenza vaccination in patients with asthma.
- Guideline developers considered inspiratory muscle training; however, they did not find sufficient evidence to evaluate the benefits of inspiratory muscle training by patients with asthma.

Drug Therapy

1. Inhaled short-acting sympathomimetics, such as salbutamol, terbutaline, fenoterol
2. Inhaled corticosteroids, such as beclomethasone, budesonide, fluticasone
3. Inhaled cromoglycate or nedocromil
4. Leukotriene antagonists, such as zafirlukast or montelukast
5. Long-acting beta-sympathomimetics, such as salmeterol or formoterol
6. Therapeutic trial with leukotriene inhibitor, theophylline, or beta-sympathomimetic tablets
7. Inhaled steroid, long acting beta-sympathomimetic drug and short-acting sympathomimetic in combination with one or more of the following drugs: leukotriene blocker, (zafirlukast or montelukast); long-acting theophylline; beta-sympathomimetic in liquid form administered with a nebuliser, inhaled anticholinergic drug (ipratropium or oxitropium); cromoglycate or nedocromil
8. Addition of oral corticosteroids (prednisolone, methylprednisolone) to combination therapy listed above.

9. Other drug treatments for asthma (antihistamines, antibiotics, antitussives, cyclosporin, methotrexate)
10. Use of omalizumab to help reduce or withdraw steroids or reduce exacerbations
11. Drug delivery via aerosol using a spacer

Note:

- Guideline developers considered but did not recommend gold as an oral corticosteroid-sparing agent in asthma.
- Guideline developers considered the effect of treatment for gastro-esophageal reflux on asthma in adults and children but found no evidence of overall improvement.
- Guideline developers considered azathioprine as a steroid-sparing agent in asthma, but found no evidence to support this use.

Monitoring Response and Follow-up

1. Pulmonary function tests (peak expiratory flow rate [PEF], forced expiratory volume in one second [FEV1])
2. Monitoring diurnal variations in asthma symptoms
3. Monitoring the frequency of exacerbations

MAJOR OUTCOMES CONSIDERED

- Asthma symptom scores
- Functional ability
- Need for inhaled sympathomimetics
- Values of peak expiratory flow (PEF) and forced expiratory volume in one second (FEV1)
- Side effects of drugs
- Pulmonary function after inhaled sympathomimetic
- Reduction in the number of hospitalizations, emergency room visits, or unscheduled visits to the doctor
- Days off from work or school
- Nocturnal asthma
- Number and severity of relapses
- Quality of life scores
- Cardiopulmonary fitness (increase in maximum oxygen uptake)
- Exercise capacity, endurance, walking distance, dyspnea during exercise
- Reduction in the need for steroids

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The evidence reviewed was collected from the Cochrane database of systematic reviews and the Database of Abstracts of Reviews of Effectiveness (DARE). In addition, the Cochrane Library and medical journals were searched specifically for original publications.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Levels of Evidence

- A. Strong research-based evidence. Several relevant, high-quality scientific studies with homogeneous results.
- B. Moderate research-based evidence. At least one relevant, high-quality study or multiple adequate studies.
- C. Limited research-based evidence. At least one adequate scientific study.
- D. No scientific evidence. Expert panel evaluation of other information.

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Not stated

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

The levels of evidence [A-D] supporting the recommendations are defined at the end of the "Major Recommendations" field.

Aims

- Teach the patient self-management in the follow-up and treatment (Gibson et al., 2002) [A].
- The patient's own primary care physician checks the adequacy of the treatment regularly.
 - Minimal symptoms
 - Normal functional ability
 - Minimal need for an inhaled sympathomimetic drug
 - Minimal daily variation in the peak expiratory flow (PEF) values (maximum 10 to 20%)
 - No side-effects of drugs
 - Normal pulmonary function at least after inhaled sympathomimetic
- Diagnose sinusitis as a potential cause of an exacerbation.

Principles of Long-Term Management

- Anti-inflammatory drugs (corticosteroids) are an essential part of the treatment (Adams, Bestall, & Jones, 2002; van Grunsven et al., 1999; DARE-990806, 2000; Haahtela et al., 1991; Reed et al., 1998) [A].
- Teaching and monitoring the inhalation technique of drugs is important.
- The treatment should be tailored for each patient according to the severity of the disease and modified flexibly step-by-step. Self-management of drug dosing is encouraged (written instructions!).
- Short courses of oral corticosteroids are occasionally needed.
- All persons with asthma should avoid exposure to high allergen concentrations (Hammarquist, Burr, & Gotzsche, 2002) [D] and sensitizing chemicals at work.
- Aspirin and other nonsteroidal anti-inflammatory drugs (NSAIDs) should be used cautiously, as 10 to 20% of patients with asthma are allergic to these drugs.
- Beta-blockers often exacerbate the symptoms of asthma.
- Smoking may wreck the results of asthma care.
- Desensitisation therapy may help some patients (Abramson, Puy, & Weiner, 2002; Malling, 1998; DARE-981030, 2000) [A].

Implementation of Long-Term Management

1. The patient has symptoms only occasionally (not every week), and they do not disturb sleep:

- Allergy proofing of the environment (Hammarquist, Burr, & Gotzsche, 2002) [D] and cessation of smoking
 - Inhaled short-acting beta-sympathomimetic as needed (Walters & Walters, 2002) [B] (salbutamol, terbutaline, or fenoterol)
2. If inhaled sympathomimetics are needed several times a week or if sleep is disturbed by asthma, adding regular anti-inflammatory medication is indicated:
- Inhaled (Mash, Bheekie, & Jones, 2002) [B] corticosteroid (beclomethasone, budesonide [Adams, Bestall, & Jones, "Budesonide," 2002] [A], or fluticasone [Adams, Bestall, & Jones, "Inhaled fluticasone propionate," 2002; Adams, Bestall, & Jones, "Inhaled fluticasone at different doses," 2002] [A]) 100 to 400 micrograms twice daily:
 - The most effective anti-inflammatory medication (Adams, Bestall, & Jones, "Inhaled beclomethasone versus placebo," 2002; van Grunsven et al., 1999; DARE-990806, 2000; Haahtela et al., 1991; Reed et al., 1998) [A]
 - Pressurized aerosols should not be used without an inhalation chamber.
 - Inhalation powders are usually well tolerated; however, patients with weakened respiratory muscles or lowered vital capacity should preferably take their drugs as dose aerosols using a spacer.
 - A leukotriene antagonist (e.g. montelukast 10 mg daily, or zafirlukast 20 mg twice daily [Kelloway, 1997; DARE-971168, 1999] [A]) may be used as an alternative, but the effect in usual licensed doses is inferior to inhaled corticosteroids.
 - Inhaled cromoglycate 5 to 20 mg four times daily or nedocromil 4 mg 2 to 4 times daily are alternatives.
 - These drugs are usually not as effective as inhaled corticosteroids.
 - There is no evidence that antileukotrienes would have an inhaled steroid-sparing effect (Kanniess, et al., 2002). Evidence on the benefit from doubling the dose of inhaled corticosteroids is insufficient. Antileukotrienes at high doses (2-4 times those recommended) used as add-on therapy to inhaled corticosteroids reduce exacerbations that require systemic steroids (Ducharme, 2002) [C].
3. If the symptoms continue daily, if the need for an inhaled sympathomimetic is frequent, and obstruction is present according to PEF monitoring:
- Check the inhalation techniques, recognize any factors that might worsen the asthma, and verify the patient's compliance.
 - Add a long-acting inhaled sympathomimetic (Walters, Walters, & Gibson, 2003) [A] (salmeterol 50 micrograms twice daily, formoterol 12–24 micrograms twice daily) without omitting the necessary anti-inflammatory medication.
4. If the long-acting beta-sympathomimetic drug is not effective or is not tolerated, discontinue it and make a therapeutic trial with leukotriene antagonist (Bjermer, et al., 2003) [B], or theophylline 200 to 300 mg at night.
5. If the symptoms are not controlled adequately with a combination of an 800 microgram daily dose of inhaled steroid and a long-acting beta-

sympathomimetic drug, added with a short-acting sympathomimetic when needed, add one or more of the following:

- Daily dose of inhaled steroid temporarily up to 2mg
- Leukotriene antagonist, montelukast or zafirlukast (Ducharme, 2002) [C]
- Long-acting theophylline 200 to 300 mg at night
- Beta-sympathomimetic in liquid form administered with a nebulizer
- Inhaled anticholinergic drug, if symptoms of chronic obstructive pulmonary disease (COPD) are present (ipratropium 80 micrograms or oxitropium 200 micrograms four times daily) (Rodrigo, Rodrigo, & Burschtin, 1999; DARE-992129, 2002) [A].
- Cromoglycate or nedocromil (effect often quite limited)
- Assess the effect of the added drug. If a favorable response is not observed within 3 to 4 weeks, the drug should be discontinued.

6. If the symptoms are not adequately controlled with the above-mentioned treatments add:

- Oral corticosteroids (prednisolone, methylprednisolone). Use the smallest dose that controls the symptoms. Corticosteroid taken every other day is usually not enough to control severe asthma in adults.

Tapering Down of Medication

- With regard to systemic adverse effects, the doses of inhaled corticosteroids that are considered safe in maintenance therapy are in adults 800 micrograms (beclomethasone, budesonide) and 400 micrograms (fluticasone).
- As the symptoms alleviate, the medication can be tapered down gradually.
- If the symptoms are minimal, if the need for inhaled bronchodilating medication is small, if the PEF values are normal, and if there is no diurnal variation, the dose of anti-inflammatory medication can be halved about 6 months after the disease has stabilized. PEF values and diurnal variation should be monitored.
- In chronic asthma it is often not possible to stop all anti-inflammatory medication.

Other Treatments for Asthma

Antihistamines

- Antihistamines have a very limited role in the treatment of asthma (Van Ganse et al., 1997; DARE-971348, 1999) [B]. They may mainly be used to alleviate other allergic symptoms.

Antibiotics

- Only clear signs of bacterial infection are an indication for antibiotics.
- Infections associated with acute exacerbations of asthma are often of viral origin. Remember sinusitis, but avoid unnecessary antibiotics.

Cough Medicines

- Cough and sputum are usually signs of poor asthma control. Intensification of the treatment or a short course of oral corticosteroids may be more effective than cough medicines.

Course of Oral Corticosteroids

Indications

- Increasing symptoms and decreasing PEF values over consecutive days
- The effect duration of inhaled bronchodilating medication is shortening.
- PEF values are less than 50 to 70% of the patient's best values.
- Sleep is disturbed by asthma.
- Morning symptoms persist until noon.
- Maximal medication without oral corticosteroids shows an insufficient effect.
- An acute exacerbation for which the patient has received nebulised or intravenous bronchodilating medication in an emergency setting (Rowe et al., 2002) [A].

Dosage

- Prednisolone is given 30 (--40) mg daily until the symptoms are alleviated and the PEF values have normalised, and still for 3 days thereafter, (usually 30 to 40 mg for 5 to 10 days).
- The drug can usually be stopped at once without tapering the dose gradually.

Self-Management of Asthma

- The patient should have good knowledge of self-management.
- The components of successful self-management are:
 - Acceptance and understanding of asthma and its treatment
 - Effective and compliant use of drugs
 - A PEF meter and follow-up sheets at home
 - Written instructions for different problems
- As a part of guided self-management the patient may receive a PEF follow-up sheet with individually determined alarm thresholds and the following instructions (Lahdensuo et al., 1996) [B]:
 - If the morning PEF values are 85% of the patient's earlier optimal value, the dose of the inhaled corticosteroid should be doubled for two weeks.
 - If the morning PEF values are below 50 to 70% of the optimal value, the patient can start a course of prednisolone 40 mg daily for one week and contacts the doctor or asthma nurse by telephone

Indications for Specialist Consultation

- The indications for consultation are relative and they depend on the services available and the experience of the patient's primary care doctor in the treatment of asthma:
 - Newly diagnosed patients
 - Suspected cases of occupational asthma
 - Recurrent exacerbations

- Assessment of working ability
- Severe exacerbation
- Symptoms in spite of a large dose of inhaled corticosteroids
- Nebuliser for home use is considered
- Pregnant women with increased symptoms
- Asthma interferes with the patient's way of living (e.g., sports activities)

Follow-up

- Because asthma is a common disease it should be mainly treated and followed up by a general practitioner.
- A patient on medication should meet his/her own doctor regularly.
- In mild cases one follow-up appointment yearly is sufficient.
- In addition to symptom history and lung auscultation, a two-week recording of PEF values at home is often sufficient as follow-up, eventually complemented by a simple spirometry (see the Evidence Based Medicine guideline on Pulmonary function tests)

Related Evidence

- There is not enough evidence to evaluate the benefits of influenza vaccination in patients with asthma (Cates, Jefferson, & Bara, 2002) [D].
- Physical training in patients with asthma improves cardiopulmonary fitness but does not change lung function (Ram, Robinson, & Black 2002; Cambach et al., 1999; DARE-990269, 2000) [B].
- There is limited evidence that breathing exercises may be of some benefit in asthma (Holloway & Ram, 2002) [C].
- There is insufficient evidence of the effectiveness of inspiratory muscle training on clinically relevant outcomes in asthma (Ram, Wellington, & Barnes, 2003) [D]
- Methotrexate may have a small steroid sparing effect in adults with asthma who are dependent on oral corticosteroids (Davies, Olson, & Gibson, 2002; Marin, 1997; DARE-970922, 1999) [B].
- Use of cyclosporin may reduce the need of oral steroids in asthma but side effects are common (Evans, Cullinan, & Geddes, "Cyclosporin," 2002) [C].
- Gold may reduce the need of steroids in asthma, but given the side effects and necessity for monitoring, the treatment cannot be recommended (Evans, Cullinan, & Geddes, "Gold," 2002) [C].
- There is no overall improvement of asthma following treatment of gastro-oesophageal reflux (Gibson, Henry, & Coughlan, 2002; Field & Sutherland, 1998; DARE-981289, 2000) [C].
- Inhaled corticosteroids are as effective as a daily dose of 7.5 to 10 mg of prednisolone, probably with fewer adverse effects (Mash, Bheekie, & Jones, 2002) [B].
- Inhaled beclomethasone has a small dose-response effect (Adams, Bestall, & Jones, "Inhaled beclomethasone at different doses," 2002) [B].
- Doses of fluticasone in the range of 100 to 1,000 micrograms are more effective than placebo in the treatment of asthma, low doses being almost as effective as high doses in mild-moderate asthma (Adams, Bestall, & Jones, "Inhaled fluticasone propionate," 2002; Adams, Bestall, & Jones, "Inhaled fluticasone at different doses," 2002) [A].

- Higher potency compounds such as fluticasone may be more effective, but there is an excess of systemic activity with fluticasone propionate compared with other inhaled corticosteroids when therapeutically effective doses are compared (Adams, Bestall, & Jones, "Fluticasone versus beclomethasone," 2002; Lipworth & Wilson, 1998; DARE-990283, 2001) [A].
- Nedocromil sodium is as effective as cromoglycate for exercise-induced asthma (Kelly, Spooner, & Rowe, 2002) [B].
- Mast-cell stabilizers (nedocromil and cromoglycate) are more effective than anticholinergics but less effective than beta-agonists in the prevention of exercise-induced bronchoconstriction (Spooner, Spooner, & Rowe, 2003) [A]
- Long acting inhaled beta-agonists have better physiological and clinical outcomes than short acting beta-agonists in regular treatment of asthma (Walters, Walters, & Gibson, 2002) [A].
- Salmeterol has a superior safety and efficacy profile compared to theophylline in chronic asthma (Davies, Brooks, & Devoy, 1998; DARE-980610, 2000)[A]
- There is insufficient evidence to compare the effectiveness of holding chambers versus nebulisers in chronic asthma. In the single high quality study, budesonide in high dose delivered by the particular nebuliser was more effective than budesonide 1600 micrograms via a large volume spacer (Cates, Adams, & Bestall, 2002) [D].
- Omalizumab is more effective than placebo at helping to reduce or withdraw inhaled steroids and at reducing asthma exacerbations (Walker, et al., 2003)[A].
- There is no evidence to support the use of azathioprine in the treatment of chronic asthma as a steroid sparing-agent (Dean, et al., 2004) [D]

Definitions:

Levels of Evidence

- A. Strong research-based evidence. Several relevant, high-quality scientific studies with homogeneous results.
- B. Moderate research-based evidence. At least one relevant, high-quality study or multiple adequate studies.
- C. Limited research-based evidence. At least one adequate scientific study.
- D. No scientific evidence. Expert panel evaluation of other information.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

REFERENCES SUPPORTING THE RECOMMENDATIONS

[References open in a new window](#)

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

Concise summaries of scientific evidence attached to the individual guidelines are the unique feature of the Evidence-Based Medicine Guidelines. The evidence

summaries allow the clinician to judge how well-founded the treatment recommendations are. The type of supporting evidence is identified and graded for select recommendations (see the "Major Recommendations" field).

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate long-term management of asthma

POTENTIAL HARMS

Drugs used in the treatment of asthma can cause side effects. The following adverse effects of therapy were reported in individual trials:

- Theophylline: Headache, nervousness, insomnia, gastrointestinal distress
- Beclomethasone: Oropharyngeal candidiasis, hoarseness, reduction in morning plasma cortisol levels before and after cosyntropin; reduction in rate of growth of children
- Antihistamines: Sedation
- Methotrexate: Hepatotoxicity
- Cyclosporin: Increased diastolic blood pressure, nausea, vomiting, paresthesia, hypertrichosis
- Triamcinolone acetonide: Adrenal suppression
- Fluticasone: Excess of systemic activity compared with other inhaled corticosteroids

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Finnish Medical Society Duodecim. Long-term management of asthma. In: EBM Guidelines. Evidence-Based Medicine [CD-ROM]. Helsinki, Finland: Duodecim Medical Publications Ltd.; 2004 Apr 8 [Various]. [103 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2001 Jan 4 (revised 2004 Apr 8)

GUIDELINE DEVELOPER(S)

Finnish Medical Society Duodecim - Professional Association

SOURCE(S) OF FUNDING

Finnish Medical Society Duodecim

GUIDELINE COMMITTEE

Editorial Team of EBM Guidelines

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Primary Author: Timo Keistinen

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Finnish Medical Society Duodecim. Long-term management of asthma. In: EBM Guidelines. Evidence-Based Medicine [CD-ROM]. Helsinki, Finland: Duodecim Medical Publications Ltd.; 2003 Oct 11 [Various].

GUIDELINE AVAILABILITY

This guideline is included in a CD-ROM titled "EBM Guidelines. Evidence-Based Medicine" available from Duodecim Medical Publications, Ltd, PO Box 713, 00101 Helsinki, Finland; e-mail: info@ebm-guidelines.com; Web site: www.ebm-guidelines.com.

AVAILABILITY OF COMPANION DOCUMENTS

None available

PATIENT RESOURCES

None available

NGC STATUS

This summary was completed by ECRI on August 28, 2001. The information was verified by the guideline developer as of October 26, 2001. This summary was updated by ECRI on December 9, 2002. This summary was verified by the developer on April 2, 2003. This summary was most recently updated by ECRI on July 1, 2004.

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